

## Response to question 119

### Question 119

*In study ID 27501, radioactive residues of  $^{14}\text{C}$ -pradofloxacin were determined in a number of tissues by quantitative whole body radiography, but not in gingival tissue, which is one of the target tissues for pradofloxacin. The Applicant is asked to provide data for gingival tissue, if the autoradiograms are still available.*

### Response

During the production of rat sections for autoradiography it is technically very difficult, if not impossible, to cut also the teeth with the microtome, since the very hard adamantine would damage the blades of the instrument. Therefore, the teeth had to be extracted from the carcass with a dental drill before the head of the rats – and the gingival tissue – could be subjected to the sectioning procedure of the autoradiography test. During the extraction of teeth, substantial amounts of gingival tissue are also removed. Hence, only limited information can be derived from the autoradiogrammes for gingival tissue.

The electronic data from the autoradiography and the scanned pictures of the rat sections are still available in the testing facility. These data were reviewed for detection of remaining gingival tissue in the sections and in the autoradiogrammes. During the inspection, some remains of gingival tissue could be detected in the sections of the rat sacrificed 4 hours after oral dosage of  $^{14}\text{C}$  pradofloxacin. The autoradiogrammes and the pictures of the sections for the dental region are shown on the following page.

The gingival tissue and remains of the root of the tooth shows a higher blackening than surrounding tissues and carcass, which is indicating a higher concentration of the compound in the gingival tissue than in the carcass of the rat. Therefore, it can be concluded that  $^{14}\text{C}$  pradofloxacin (BAY 14-1877) is present at a significant concentration in the gingival tissue of rats.

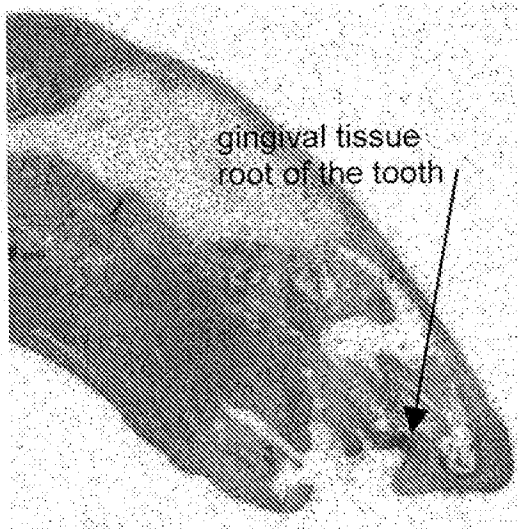
## Autoradiogrammes and section of rat gingival tissue

Zoomed detail of Figure 19 in report MR210/01 compared to zoomed detail of a scanned picture of the animal section used for autoradiography.

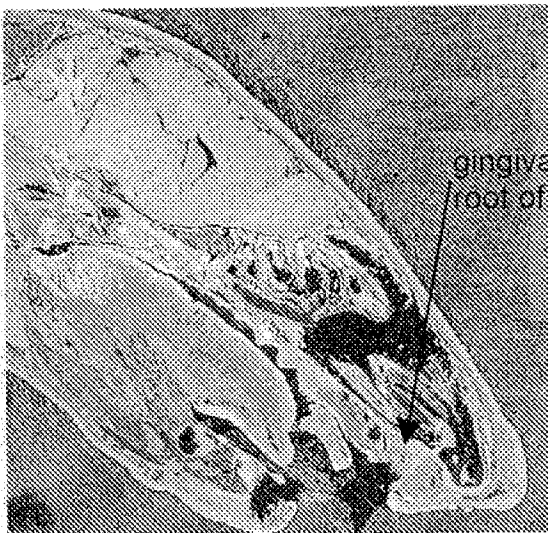
Animal no. 649 (sacrifice 4h after a single oral administration of [2-14C]BAY-14-1877 (3<sup>rd</sup> section from left)

Autoradiogramme

Scanned Rat Section



gingival tissue  
root of the tooth



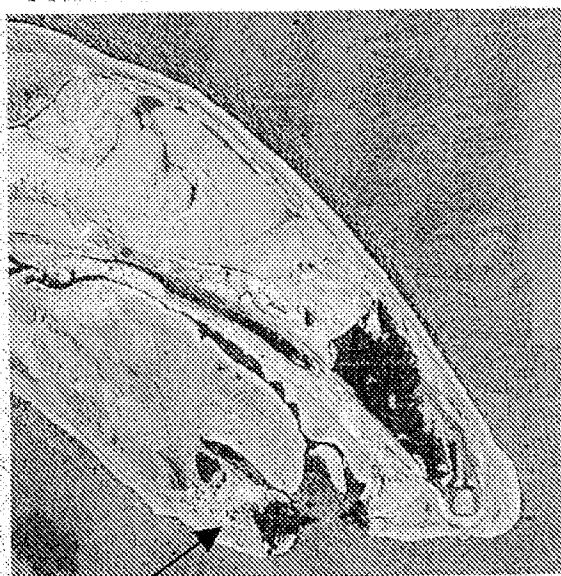
gingival tissue,  
root of the tooth

Zoomed detail of Figure 19 in report MR210/01 compared to zoomed detail of a scanned picture of the animal section used for autoradiography.

Animal no. 649 (sacrificed 4h after a single oral administration of [2-14C]BAY-14-1877 (4<sup>th</sup> section from left)

Autoradiogramme

Scanned Rat Section



gingival tissue + root of the tooth